Supplementary S3. Results from Individual Studies

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
Survival/Mortality								
Abe[24]	22.6%) had CI (7/31) CI N=4 Mild (MMSE: 20-23) N=3 Moderate (MMSE: 14-19)	1-year Overall Survival	1 year	NR	N	1-year OS of patients with CI was 0%. In univariate analysis model, CI[a] was not associated with 1-year OS (p=0.1384) (no other estimates provided)	N/A	N/A
Aldricks[25] (2011)	10% (21/202) had CI (MMSE <=24):	Mortality	Median 9 months (1-33)	NR	N	Model 1: HR 0.99 (0.48-2.07) Model 2: HR 0.92 (0.44-1.93)	N/A	N/A
Aaldriks (2013a)[26]	13% (19/143) suspect for cognitive decline (IQ-CODE >3.31 pts)	Mortality	Median 15 months (0.5-62)	16% patients received reduced dose (reason not known. It is not reported how many % of which were patients with CI)	N	Adjuvant group: HR 3.08 (0.76-20.93) Palliative group: HR 1.51 (0.59-3.85)	N/A	N/A

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	8% (11/143) had CI (MMSE <= 24 pts):							
Aaldriks (2013b)[27]	9% (5/55) had CI (MMSE <= 24 pts): 18% (10/55) had CI (IQCODE >= 3.3)	Mortality	Median 11 months (0-57)	NR	N	MMSE: HR 1.68 (0.49-5.78) IQCODE: HR 1.07 (0.49-2.37)	N/A	N/A
Aaldriks (2016)[28]	12.9% (62/494) suspect for cognitive decline (IQ-CODE >3.31 pts) 9% (44/494) had CI (MMSE <= 24 pts)	Mortality	Time between first geriatric assessment (window from May 2004-Feb 2010) and January 1, 2013, or the date of death	NR	N	MMSE: 1.36 (0.97-1.91) IQCODE: 1.12 (0.83-1.50)	N/A	N/A

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Biesma[30] (2011)	NR	Survival	Median 21.0 months	NR	N	HR 0.95 (0.83-1.09)	N/A	N/A
Dubruille[31] (2015)	31% (28/90) had CI (MMSE <27) 51% (46/90) had CI (MoCA <26) Patients with dementia	One-year survival	1 year	Initial treatment choice: 66% received full dose, 34% received reduced ode. However, unclear how many CI patients received which dose.	Y	Cognitive status (HR = 3.260, 95% CI: 1.043-10.194; p = 0.042) were predictive of OS 1-year OS was 63% for patients with CI versus 88% for those without.	Y	Age, gender, diagnosis, disease status, ECOG, initial treatment choice, tolerance to treatment

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	were excluded							
Falandry[33] (2013a)	29% (32/111) had CI (MMS <25)	Overall survival	Median 16.4 months (0.2-49.6 months)	Patients received carbo dosed at AUC 5mg/ml/min for 30 min q3 week up to 6 cycles	N	MMSE score >24 was associated with increased survival: HR 1.08, p=0.79 (no confidence interval provided)	N/A	N/A
Falandry[34] (2013b)	Five words recall: mean 18.5 (SD 3.4) (no other details provided)	Progression free survival (PFS) and overall survival	24 months	Did not mention\n\nOnly said 6 courses of "adapted dose of pegylated liposomo doxorubisin(40mg/m Q28 days)"	N	NR	N/A	N/A
Hamaker[35]	7% MMSE<=23	Survival	24 months	NR	Y\n\nN	Univariate model:\nHR 3.74 (1.43-9.73)\nMultivariate model: HR 1.88 (confidence interval not provided)	Y	Age, performance status, chemotherapy type

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
Hshieh[3] (2018)	35.3% (127/360) had probable executive dysfunction (CIB score <5); 17.2% (62/360) had probable working memory impairment (<= 2 words in 5-word delayed recall	Survival	1 year	65.6% percent of sample underwent intensive treatment: among this group decreased survival was seen for probable impairment For both tests.	Y	Patients with impaired working memory had worse median survival (10.9 [SD 12.9] vs 12.2 [SD 14.7] months; log rank p< .001), including when stratified by indolent cancer (log rank p = .01) and aggressive cancer (p < .001), and in multivariate analysis when adjusted for age, comorbidities, and disease aggressiveness (adds ratio, 0.26; 95% CI, 0.13-0.50). Impaired working memory was also associated with	Y	Age, comorbidity, cancer aggressiveness

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						worse survival for those undergoing intensive treatment (log-rank $p < .001$) Executive dysfunction was associated with worse survival only among patients who underwent 'intensive treatment' (log-rank $p = .03$)		
Klepin[36] (2013)	28.8% had CI (3MS** < 77)	Overall survival	30 days	No mention of dose reduction	Y	Impaired cognition was associated with worse overall survival Unadjusted HR 2.4 (95% CI: 1.3-4.4) Adjusted^^ HR 2.5 (95% CI: 1.2-5.5)	Y	Age, gender, ECOG, cytogenic risk group, MDS, hemoglobin

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						median OS for patients with CI was 5.2 months compared to 15.6 months for those without impairment		
Lee[44] (2020)	28.3% had dementia (no details on assessment tool used)	Overall survival	Median 15.4 months (0.3-107.6)	Unclear	N	No significant difference was found between survivor group and non-survivor group in terms of cognitive status (p=0.168). Confidence interval not provided	N/A	N/A
Molga[38] (2019)	11% had CI (MMSE < 24)	Overall survival	Varied	N	N	HR 1.08 (0.38-3.02) Analysis of OS of those who could not complete 6 cycles included 8 patients – the 4	N/A	N/A

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
						with CI and 4 others without CI). The 4 patients with CI stopped due to comorbidities or intercurrent illness; whereas patients without CI stopped due to lack of response/disease progression		
Robb[39] (2009)	Case control study: case: n=86 Control: n=172 Among the cases, a cutoff of <=20 was used to delineate mild vs. moderate-to-severe	Survival	N/A (case-control)	NR	Y	Non-CI group had greater survival (Mdn = 72.6 months) than CI group (Mdn = 23.0 months); $p<.001$ Cognitive status was an independent predictor of survival (p=.045) (other estimates not available)	Y	Baseline ECOG, ADLs/IADLs, CIRS-G, Charlson scores, GDS score, age, and gender

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
Soubeyran[41] (2012)	19% had CI (MMSE <= 23)	Mortality (early death risk [defined as within 6 months])	6 months	14.9% received standard reduced treatment 40.2% received adapted treatment Unclear how many of whom among these groups had CI	Y N	Significant in univariate model (P = .012) (actual magnitude effects not provided) Not significant in multivariate model adjusting for treatment site (details NR)	Y	Treatment site
Thibaud[42] (2021)	31% had CI (MMSE <27)	Survival	12 months	65% received standard dose: 35% received reduced dose. Unclear whether or how many CI patients had reduced dose	Y	Cognitive impairment (MMSE < 27) predicted one-year survival (HR 1.82 [95% CI 1.13-2.91], p = 0.01) (actual magnitude of effects not provided)	Y	*"impact of disease itself and other vulnerabilities"*
Wildes[43] (2013)	4.8% (3/63)	Mortality	Median 20 months (0.01-47 months)	n=1 received dose reduction due to renal impairment	N	HR 0.83 (0.11-6.23)	N/A	N/A

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
	Short Blessed score >9							
Chemotherapy completion								
Abe[24] (2011)	22.6% had CI: N=4 Mild (MMSE: 20-23) N=3 Moderate (MMSE: 14-19)	Complete remission (CR) Unplanned endpoint: discontinuation of consolidation chemotherapy	3 year	All 7 alzeihmers pateints received (donezepezil hydrochloride, drug therapy for BPSD, and support by family during chemotherapy. No mention of dose reduction	Unclear	All 7 patients with CI were able to receive chemotherapy through administration of donepezil hydrochloride, and family support during chemotherapy administration. CR was achieved in the 3 moderate cases CI. However, consolidation chemotherapy was discontinued in all 7 patients with CI due to	N/A	N/A

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
						exacerbation of BPSD		
Aaldriks[28] (2016)	12.9% had suspect for cognitive decline (IQ-CODE >3.31 pts) 9% had CI (MMSE <= 24 pts): 9%	Chemotherapy completion (>= 4 cycles)	Time between first geriatric assessment (window from May 2004-Feb 2010) and January 1, 2013, or the date of death	It was only reported that patients stated chemotherapy. No mention of dose reduction	N	Univariable analysis: IQCODE: OR 0.96 (0.53-1.75) MMSE: OR 1.65 (0.87-3.13)	N/A	N/A
Aldricks[25] (2011)	11% had CI (MMSE <=24) 15% had CI (IQCODE >3.31)	Chemotherapy completion	Unclear	NR	Y	Compared to those who received >=4 cycles of chemotherapy, MMSE scores were significant lower for patients who received <4 cycles (p=0.04)	N/A	N/A

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
						(other estimates not available) Among those with CI (IQCODE >3.31), 20% underwent <4 cycles whereas 13% underwent >=4 cycles (p=0.2). Among those with CI (MMSE <= 24), 11% underwent <4 cycles whereas 3% underwent >=4 cycles (p=0.04).		
Laurent[37] (2014)	12.3% had CI (MMSE<24)	Chemo discontinuation? (Chemo feasibility??)	Median 13.4 months (5.3-24.6)	NR	Y	Higher MMSE (median 28 (27-30]) significant in univariate analysis (p = .05)	Y	Functional status, mobility limitation f

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
					N	(actual absolute magnitude of effects not provided) Not significant in multivariate model (details on estimates not provided)		
Molga[38] (2019)	11% had CI (MMSE <24)	Chemotherapy completion	50 months	It was mentioned there was no change in planned treatment due to geriatric deficits.	Y	Patients with CI completed significantly less azacitidine cycles compared to those without CI (3.5 ± 2.1 vs. 10.9 ± 7.9; p=0.34) A higher number of patients with CI (3/4; 75%) could not completed 6 cycles of azacitidine compared to patients without	N/A	N/A

Author/year	Proportion with and/or Degree of cognitive impairment	Endpoint outcome(s) examined	Duration of follow-up	Baseline dose reduction (Y/N)	Found significant (Y/N)	Details	Multivariate model performed for CI (Y/N)	Adjusted for in MV
						CI (5/21; 24%) (p = .05).		
Wildes[43] (2013)	4.8% had severe CI (Short Blessed score >9)	Chemo completion	Median 20 months (0.01-47 months)	n=1 received dose reduction due to renal impairment	N	OR 0.71 (0.06-8.46)	N/A	N/A
Chemotherapy toxicity								
Aparicio[29] (2013)	31% had CI (MMSE <= 27)	Treatment toxicity (at least one grade 3-4 toxicity)	The three outcomes were analyzed during the first 4 months of starting treatment	Randomized to FU-based chemotherapy alone or in combination with IRI. In the IRI arm, first 2 cycles were 150mg/m of IRI, and increased in the absence of toxicity in subsequent cycle.	Y	MMSE (<=27) was significant predictive factor in multivariate analysis for grade 3-4 toxicity (OR 3.84; 95% CI: 1.24-11.84) In patients with MMSE <=27/30, 89% 9n=17) in the IRI arm had grade 3-4 toxicity versus 50% (n=9) in the FU arm. In patients with an MMSE >27/30,	Y	NR

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						58% (n=15) in the IRI arm had grade 3-4 toxicity versus 30% (n=8) in the FU arm		
Extermann[32] (2012)	MMS score mean 28 (15-30) Patients with dementia were excluded	Chemotherapy toxicity	Maximum 1 month after last cycle. IF chemotherapy was continued beyond 6 months, then follow-up was ended at 6 months	Gemcitabine 1.25g/m on day 1, a, 15 Q4 weeks Chemo determined by oncologists by baseline. No mention whether patient received standard or dose-reduced treatment	Y N	Association present for Grade 3/4 non hematologic toxicity: OR = 0.77 (0.63-0.93), p = .008 (Did not provided actual absolute magnitude of effects) Association not present for grade 4 hematologic toxicity OR 0.97 (0.87-1.07)	Y	Chemotherapy regimen

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Falandry[34] (2013b)	Five words recall Mean 18.5 (SD 3.4)	Chemo toxicity Chemo tolerance and efficacy outcomes Tumor response	24 months	NR	N	N/A	N/A	N/A
Hamaker[35] (2014)	7% had CI (MMSE<=23)	Chemotherapy toxicity	Median 32 months	No mention of any baseline dose reduction Randomized to doxorubicin 45mg/m q 4 weeks up to 6 weeks, or capecitabine 2000mg/m orally on days 1-14, every 3 weeks for up to 8 cycles	N	OR 1.14 (0.09-10.17)	N/A	N/A
Jayani[3] (2019)	36% (250/703) had potential CI (BOMC score 5-10)	Chemotherapy toxicity	?	76% received standard dose (i.e. 24% had dose reduction. However, it is not known how	Y	Potential CI (BOMC score 5-10) was associated with increased risk of severe toxicity	Y	CARG Toxicity Risk Group (low, medium, high)

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	Patients with dementia were excluded from analysis			many of whom had CI)	N	(OR 1.54, p<= 0.01). This was no longer significant after adjusting for CARG score; OR 1.98 (0.76-5.17) However, among patients with lower education level (n=258; 36.7%), potential CI remained associated with severe chemotherapy toxicity despite adjusting for CARG score (OR 1.08; p = 0.03) The incidence of severe chemotherapy toxicity was 51.0% in patients without CI whereas the		

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						incidence was 61.6% in patients with potential CI.		
Shin[40] (2012)	Mild cognitive decline (MMSC-KC <=24): 51.6% CI (MMSC-KC <16 signifies cognitive impairment): 4.7% Patients with 'significant' CI were excluded	Chemo toxicity	Mean 8.89 weeks	NR	N	Mild CI: OR 0.68 (0.18-2.63) CI: OR 1.53 (1.12-19.88)	N/A	N/A
Wildes[43] (2013)	4.8% had severe CI(	Chemo toxicity (non-hematologic)	Median 20 months (0.01-47 months)	n=1 received dose reduction due to renal impairment	Not estimable due to 0 count of	N/A	N/A	N/A

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	Short Blessed score >9)				toxicity in the cell			

^bAbe et al. referred to mild and moderate CI as 'dementia' in this study.

**modified mini mental status exam

^^ adjusting for age, gender, hemoglobin, ECOG score, prior myelodysplastic syndrome, and cytogenic group

BOMC = Blessed Orientation-Memory-Concentration test

BPSD = Behavioural and psychological symptoms of dementia

CARG = Cancer and Aging Research Group